



Application No. 10/602,693

Amendment dated August 24, 2005

Responsive to Office Action dated April 6, 2005

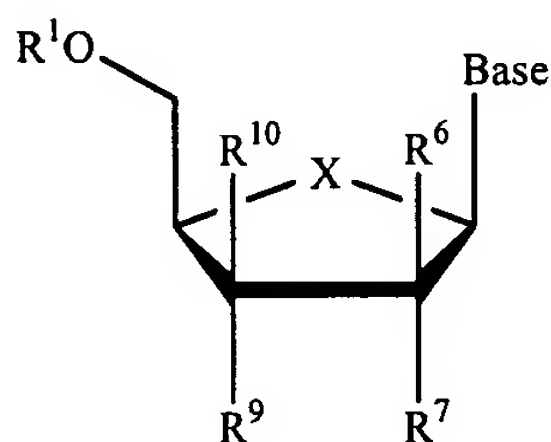
### Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims

Claims 1-88 (canceled)

Claims 89 (Currently Amended): A method for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt or ester thereof, wherein:

Base is a purine;

$R^1$  and  $R^2$  are independently H; phosphate; a stabilized phosphate prodrug; acyl; alkyl; sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents selected from hydroxyl, amino, alkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, sulfate, phosphonic acid, phosphate, phosphonate, either unprotected or protected as necessary; a lipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein  $R^1$  and  $R^2$  are independently H or phosphate;

$R^6$  is hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl,  $-C(O)O(alkyl)$ ,  $-C(O)O(lower\ alkyl)$ ,  $-O(acyl)$ ,  $-O(lower\ acyl)$ ,  $-O(alkyl)$ ,  $-O(lower\ alkyl)$ ,  $-O(alkenyl)$ , chloro, bromo, fluoro, iodo,  $NO_2$ ,  $NH_2$ ,  $-NH(lower\ alkyl)$ ,  $-NH(acyl)$ ,  $-N(lower\ alkyl)_2$ , or  $-N(acyl)_2$ ;

$R^7$  and  $R^9$  are independently hydrogen,  $OR^2$ , hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl,  $-C(O)O(alkyl)$ ,  ~~$-C(O)O(lower\ alkyl)$~~ ,  $-O(acyl)$ ,  ~~$-O(lower\ acyl)$~~ ,  $-O(alkyl)$ ,  ~~$-O(lower\ alkyl)$~~ ,  $-O(alkenyl)$ , chlorine, bromine, iodine,  $NO_2$ ,  $NH_2$ ,  $-NH(lower\ alkyl)$ ,  $-NH(acyl)$ ,  $-N(lower\ alkyl)_2$ , or  $-N(acyl)_2$ ;

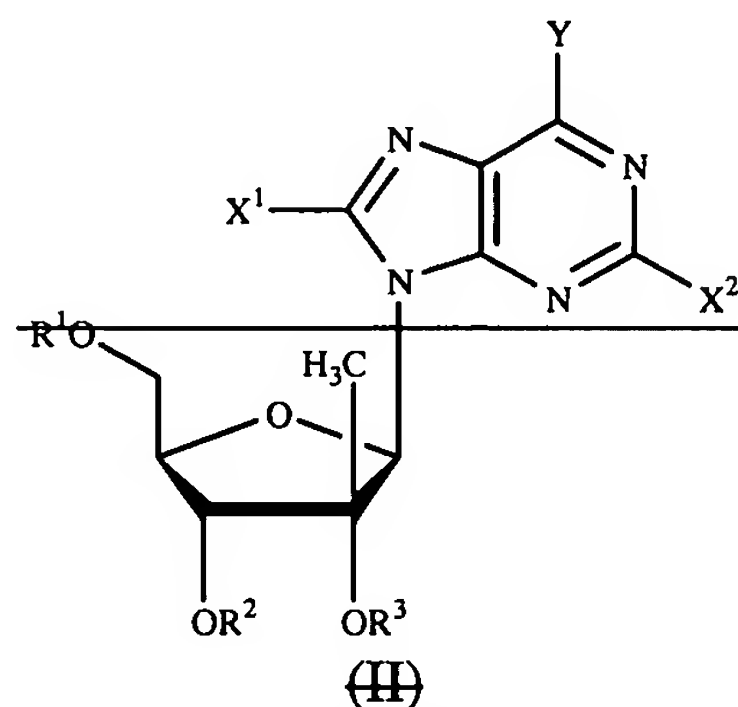
$R^{10}$  is H, alkyl, chlorine, bromine or iodine;

~~alternatively,  $R^7$  and  $R^9$ , or  $R^7$  and  $R^{10}$  can come together to form a bond; and~~

X is O, S,  $SO_2$  or  $CH_2$ .

Claims 90-129 (canceled)

Claim 130 (Currently Amended): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, wherein the base is selected from the group consisting of  $N^6$ -alkylpurine,  $N^6$ -acylpurine,  $N^6$ -benzylpurine,  $N^6$ -halopurine,  $N^6$ -vinylpurine,  $N^6$ -acetylenic purine,  $N^6$ -acyl purine,  $N^6$ -hydroxyalkyl purine,  $N^6$ -thioalkyl purine,  $N^2$ -alkylpurine,  $N^2$ -alkyl-6-thiopurine,  $C^5$ -hydroxyalkyl purine,  $N^2$ -alkylpurine,  $N^2$ -alkyl-6-thiopurine, adenine, guanine, hypoxanthine, 2,6-diaminopurine and 6-chloropurine.  
~~comprising administering an anti-virally effective amount of a compound of Formula II:~~



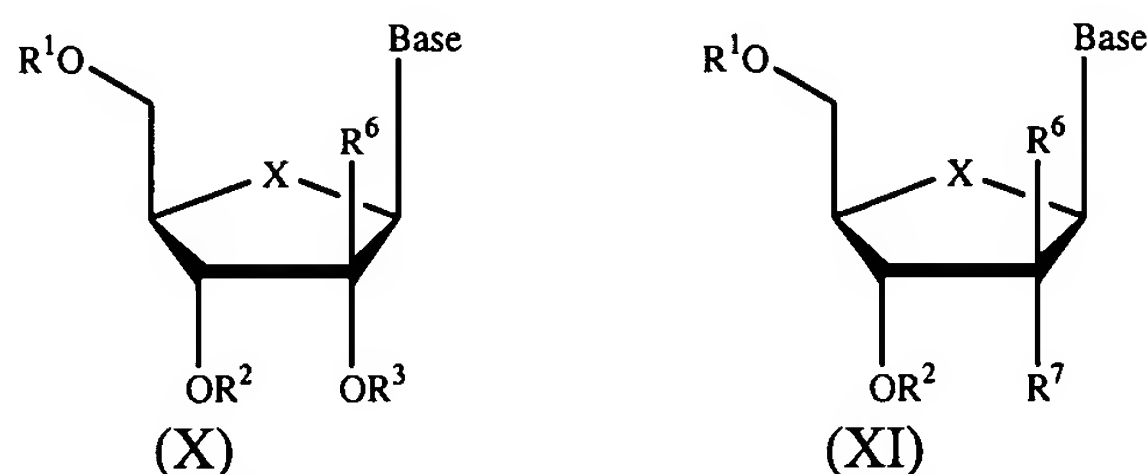
~~or a pharmaceutically acceptable salt or ester thereof, wherein:~~

~~$R^1$ ,  $R^2$  and  $R^3$  are independently H; phosphate or a stabilized phosphate prodrug; acyl; alkyl; sulfonate ester; or benzyl, wherein the phenyl group is optionally substituted with one or more substituents; a lipid; an amino acid; a carbohydrate; a peptide; cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein  $R^1$ ,  $R^2$  and  $R^3$  are independently H or phosphate; and~~

~~Y is hydrogen, bromo, chloro, fluoro, iodo,  $OR^4$ ,  $NR^4R^5$  or  $SR^4$ ;~~

~~X<sup>1</sup> and X<sup>2</sup> are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO alkyl, CO aryl, CO alkoxyalkyl, chloro, bromo, fluoro, iodo, OR<sup>4</sup>, NR<sup>4</sup>NR<sup>5</sup> or SR<sup>4</sup>; and~~  
~~R<sup>4</sup> and R<sup>5</sup> are independently hydrogen, acyl, or alkyl.~~

Claim 131 (currently amended): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula X or XI:



or a pharmaceutically acceptable salt or ester thereof, wherein:

Base is a purine;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are independently H; phosphate or a stabilized phosphate prodrug; acyl; alkyl; sulfonate ester; or benzyl, wherein the phenyl group is optionally substituted; a lipid; an amino acid; a carbohydrate; a peptide; cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are independently H or phosphate;

R<sup>6</sup> is hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), ~~-C(O)O(lower alkyl)~~, -O(acyl), ~~-O(lower acyl)~~, -O(alkyl), ~~-O(lower alkyl)~~, -O(alkenyl), chloro, bromo, fluoro, iodo, NO<sub>2</sub>, NH<sub>2</sub>, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)<sub>2</sub>, or -N(acyl)<sub>2</sub>;

R<sup>7</sup> is hydrogen, OR<sup>3</sup>, hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), ~~-C(O)O(lower alkyl)~~, -O(acyl), ~~-O(lower acyl)~~, -O(alkyl), ~~-O(lower alkyl)~~, -O(alkenyl), chlorine, bromine, iodine, NO<sub>2</sub>, NH<sub>2</sub>, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)<sub>2</sub>, or -N(acyl)<sub>2</sub>; and

X is O, S, SO<sub>2</sub> or CH<sub>2</sub>.

Claim 132 (currently amended): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, wherein, in the compound of Formula XVII:

$R^{10}$  is H, alkyl, chlorine, bromine or iodine;

$R^7$  and  $R^9$  are independently hydrogen,  $OR^2$ , alkyl, alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine,  $NO_2$ ,  $NH_2$ ,  $-NH(\text{lower alkyl})$ ,  $-NH(\text{acyl})$ ,  $-N(\text{lower alkyl})_2$ , or  $-N(\text{acyl})_2$ ;

$R^6$  is alkyl, chlorine, bromine or iodine;

~~alternatively,  $R^7$  and  $R^9$ , or  $R^8$  and  $R^9$  can come together to form a bond; and~~

X is O, S,  $SO_2$  or  $CH_2$ .

Claim 133 (previously presented): The method of claim 89 wherein  $R^1$  is hydrogen or phosphate.

Claim 134 (previously presented): The method of claim 89 wherein  $R^2$  is hydrogen, acyl or alkyl.

Claim 135 (previously presented): The method of claim 89 wherein  $R^6$  is alkyl.

Claim 136 (previously presented): The method of claim 89 wherein  $R^7$  and  $R^9$  are independently hydrogen,  $OR^2$ , or hydroxy.

Claim 137 (previously presented): The method of claim 89 wherein  $R^7$  is hydroxy.

Claim 138 (previously presented): The method of claim 89 wherein  $R^9$  is hydroxy.

Claim 139 (previously presented): The method of claim 89 wherein  $R^7$  and  $R^9$  are hydroxy.

Claim 140 (previously presented): The method of claim 89 wherein  $R^{10}$  is hydrogen.

Claim 141 (previously presented): The method of claim 89 wherein X is O.

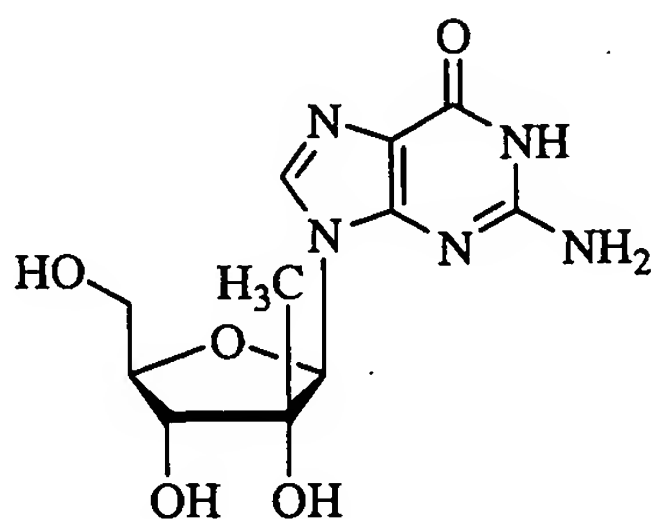
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Claim 142 (previously presented): The method of claim 89 wherein

R<sup>1</sup> is hydrogen or phosphate;  
R<sup>2</sup> is hydrogen, acyl or alkyl;  
R<sup>6</sup> is alkyl;  
R<sup>7</sup> and R<sup>9</sup> are independently hydrogen, OR<sup>2</sup>, or hydroxy;  
R<sup>10</sup> is hydrogen; and  
X is O.

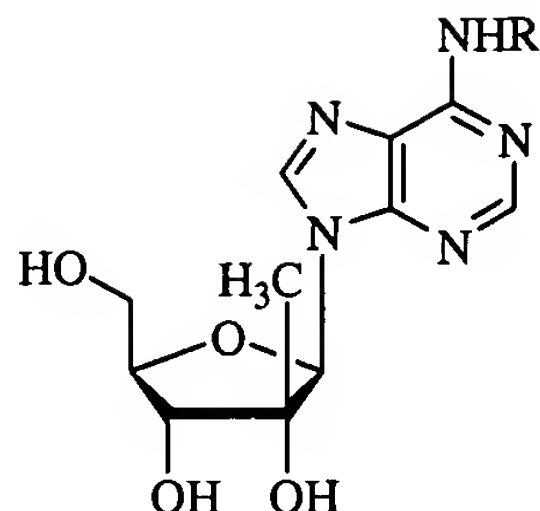
Claim 143 (Currently Amended): The method of claim 89, wherein the base is a purine selected from the group consisting of N<sup>6</sup>-alkylpurines, ~~N<sup>6</sup>-acylpurines (wherein acyl is C(O)(alkyl), (aryl), (alkylaryl), or (arylalkyl)), N<sup>6</sup>-benzylpurine, N<sup>6</sup>-halopurine, N<sup>6</sup>-vinylpurine, N<sup>6</sup>-acetylenic purine, N<sup>6</sup>-acyl purine, N<sup>6</sup>-hydroxyalkyl purine, N<sup>6</sup>-thioalkyl purine, N<sup>2</sup>-alkylpurines, N<sup>2</sup>-alkyl-6-thiopurines, N<sup>2</sup>-alkylpurines, N<sup>2</sup>-alkyl-6-thiopurines, 5-azacytidinyl, guanine, adenine, hypoxanthine, 2,6-diaminopurine, and 6-chloropurine.~~

Claim 144 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt or ester thereof.

Claim 145 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:

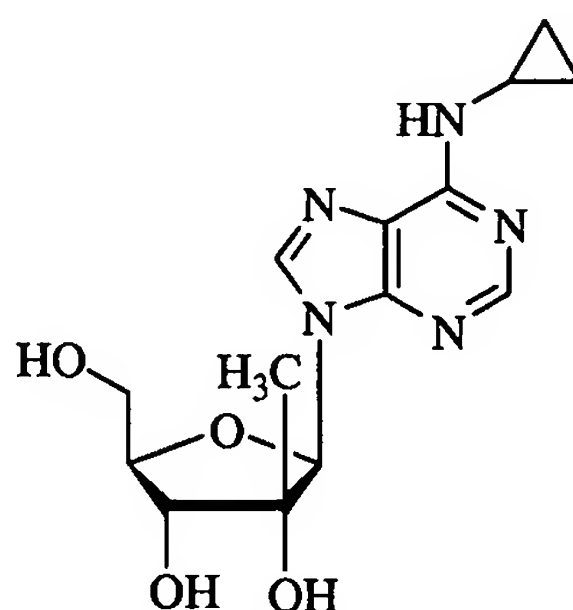


or a pharmaceutically acceptable salt or ester thereof, wherein R is hydrogen or alkyl.

Claim 146 (previously presented): The method of claim 145, wherein R is methyl, ethyl, propyl, isopropyl, or cyclopropyl.

Claim 147 (previously presented): The method of claim 146 wherein R is butyl, isobutyl, *t*-butyl, pentyl, cyclopentyl, isopentyl, or neopentyl.

Claim 148 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:

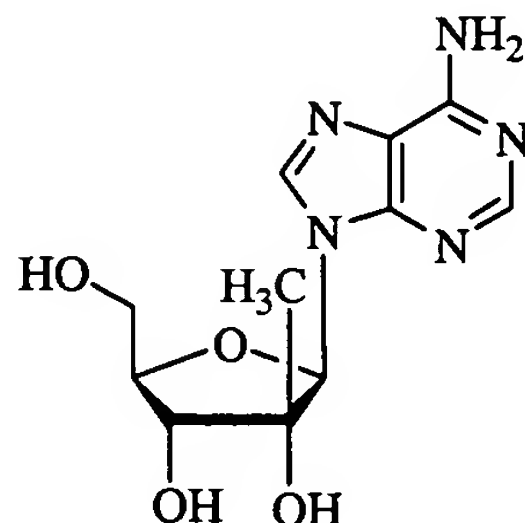


or a pharmaceutically acceptable salt or ester thereof.

Claim 149 (canceled)

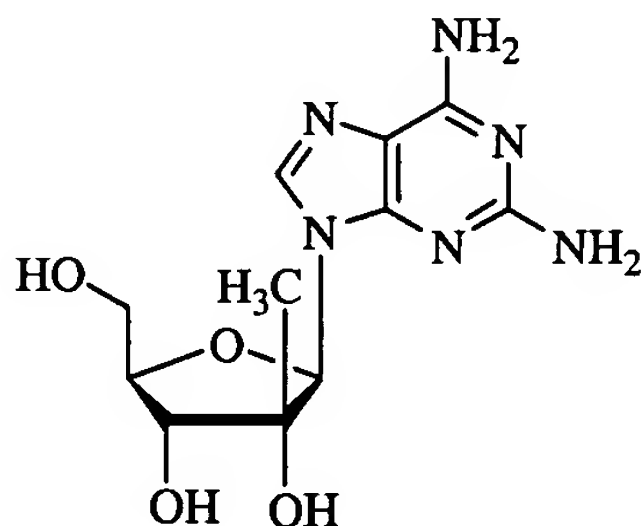
Claim 150 (canceled)

Claim 151 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt or ester thereof.

Claim 152 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:

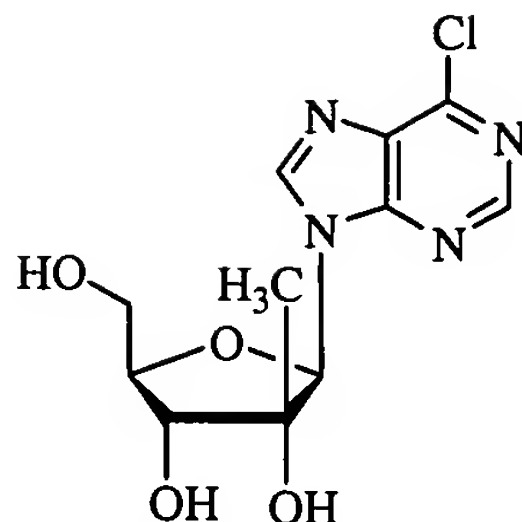


or a pharmaceutically acceptable salt or ester thereof.

Claim 153 (canceled)

Claim 154 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:

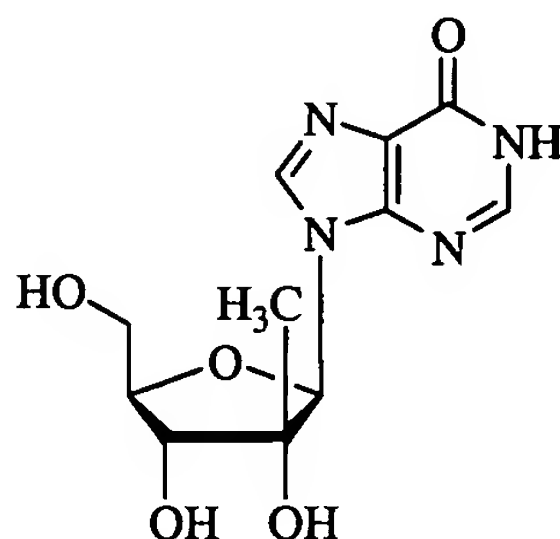
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or a pharmaceutically acceptable salt or ester thereof.

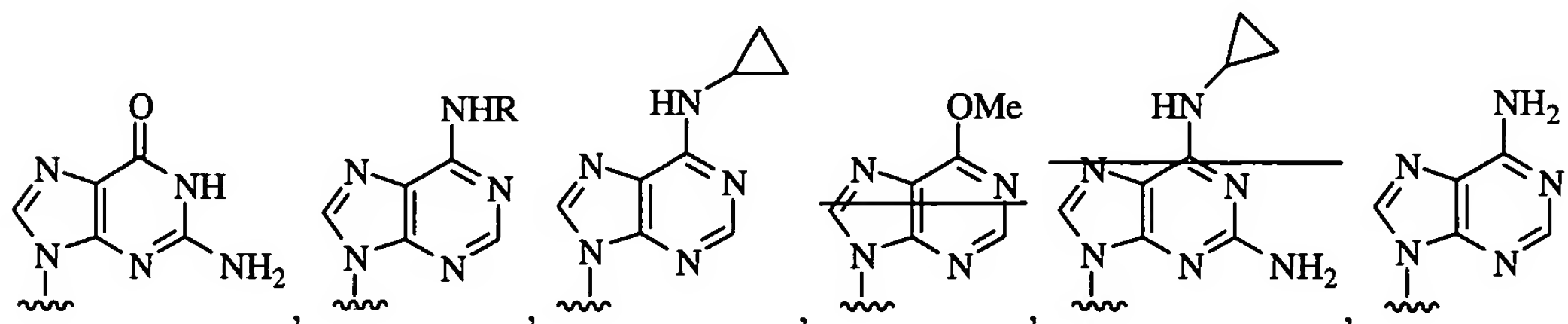
Claim 155 (canceled)

Claim 156 (previously presented): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:

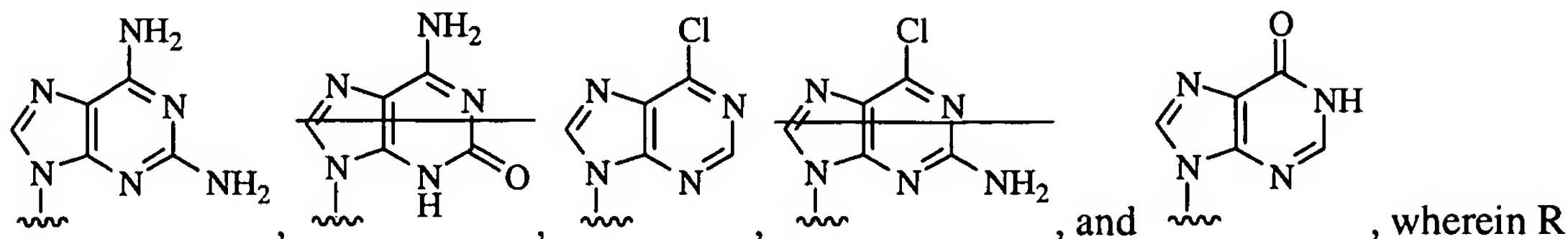


or a pharmaceutically acceptable salt or ester thereof.

Claim 157 (currently amended): The method of claim 89 for the treatment of a flavivirus or pestivirus infection in a host, wherein the purine base is selected from the group consisting of







is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *t*-butyl, pentyl, cyclopentyl, isopentyl, or neopentyl.

Claim 158 (previously presented): The method of claim 89, wherein the method comprises administering the compound or a pharmaceutically acceptable salt or ester thereof in combination or alternation with a second anti-flavivirus or anti-pestivirus agent.

Claim 159 (previously presented): The method of claim 158, wherein the second anti-flavivirus or anti-pestivirus agent is selected from the group consisting of consisting of interferon, ribavirin, a protease inhibitor, a thiazolidine derivative, a polymerase inhibitor, and a helicase inhibitor.

Claim 160 (previously presented): The method of claim 159, wherein the second anti-flavivirus or anti-pestivirus agent is interferon.

Claim 161 (previously presented): The method of claim 159, wherein the second anti-flavivirus or anti-pestivirus agent is a protease inhibitor.

Claim 162 (previously presented): The method of claim 159, wherein the second anti-flavivirus or anti-pestivirus agent is ribavirin.

Claim 163 (previously presented): The method of claim 89, wherein the compound is in the form of a dosage unit.

Claim 164 (previously presented): The method of claim 163, wherein the dosage unit contains 50 to 1000 mg of said compound.

Claim 165 (previously presented): The method of claim 163, wherein said dosage unit is a tablet or capsule.

Claim 166 (previously presented): The method of claim 89, wherein the host is a human.

Claim 167 (previously presented): The method of claim 89, wherein the compound is in substantially pure form.

Claim 168 (previously presented): The method of claim 89, wherein the compound is at least 90% by weight of the  $\beta$ -D-isomer.

Claim 169 (previously presented): The method of claims 89, wherein the compound is at least 95% by weight of the  $\beta$ -D-isomer.

Claim 170 (previously presented): The method of claim 89, wherein the flavivirus or pestivirus is a Dengue virus.

Claim 171 (previously presented): The method of claim 89, wherein the flavivirus or pestivirus is a West Nile virus.

Claim 172 (previously presented): The method of claim 89, wherein the flavivirus or pestivirus is a yellow fever virus.

Claim 173 (previously presented): The method of claim 89, wherein the flavivirus or pestivirus is a bovine viral diarrhea virus (BVDV).

Claim 174 (previously presented): The method of claim 89, wherein the flavivirus or pestivirus is not a hepatitis C virus.